REMARKS

The specification has been amended to correct inadvertent typographical and grammatical errors, and the claims have been amended to clarify the invention. The specification has been amended to delete references to certain websites regarded by the examiner as potential hyperlinks. The Table at p. 22 has been amended to clarify the numeral "6" at the intersection of column 8 and row 9 of the Table. Claim 2 has been amended to recite only elected SEQ ID NOs:1 and 8, and claims 16-20 have been canceled without prejudice. New claim 21 has been added to claim a polynucleotide encoding a polypeptide having the amino acid sequence of SEQ ID NO:14 or 15, or a naturally occurring variant of these polypeptides having at least 95% sequence identity to SEQ ID NO:14 or 15. Support for new claim 21 is found in the specification, for example, at p. 23, lines 29-30 and at p. 24, lines 18-19 and 30-31, which disclose the polypeptides of SEQ ID NO:14 and 15 as encoded by the polynucleotides of SEQ ID NO:1 and 8, respectively; and at p. 3, lines 29-30, p. 8, lines 29-31, and at p. 10, lines 16-17 which describe naturally occurring variants of the polynucleotides and polypeptides of the invention. No new matter is added by any of these amendments, and entry of the amendments is therefore requested.

Objections to the Disclosure

The Examiner has objected to the disclosure because in the table on page 22, a faint numeral "6" appears at the intersection of column 8, row 9, and if the numeral is intended, applicants should amend the application to make it clear. The table has been amended to clarify the presence of the numeral "6" at the intersection of column 8 and row 9 of the table.

The Examiner has also objected to embedded hyperlinks and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code in accordance with MPEP § 608.01.

Applicants point out that the MPEP states at § 608.01 that this policy is based on the principle that "USPTO policy does not permit the USPTO to link to any commercial sites since the USPTO exercises no control over the organization, views or accuracy of the information contained on those outside sites (underline added). Section 608.01 goes on to state that "where hyperlinks and/or other forms of browser-executable codes are a part of the applicant's invention and it is necessary to have them included in the patent application in order to comply with the

requirements of 35 U.S.C. 112, first paragraph, and applicant does not intend to have these hyperlinks as active links, examiners should not object to these hyperlinks. The Office will disable these hyperlinks when preparing the text to be loaded onto the USPTO web database (underline added). The web site recited at p. 19, line 19 is a non-commercial, government web site specifically associated with the National Center for Biotechnology Information (NCBI). In addition, Applicants further declare that the cited web site is not intended as an active hyperlink but is recited as a "freely available sequence comparison algorithms" (p. 19, line 18), and that the recitation in the application therefore complies with the requirements of the MPEP § 608.01. However, in the interests of expediting prosecution and the allowance of claims, this hyperlink, as well as another recited at p. 20 of the specification have been deleted.

Withdrawal of the objections to the disclosure is therefore requested.

35 U.S.C. § 112, Second Paragraph, Rejection of Claims 2, 3 and 13-15

The Examiner has rejected claims 2, 3 and 13-15 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant(s) regard as the invention. The Examiner stated that the claims are vague and indefinite because they include SEQ ID NOs not searched, and stated that cancellation of those sequences would overcome this part of the rejection. These sequences, SEQ ID NOs:2, 3, 5-7 and 9-13, have been deleted from the claims, and withdrawal of the rejection is therefore requested.

35 U.S.C. § 112, First Paragraph, Rejection of Claim 15

The Examiner has rejected claim 15 under 35 U.S.C. § 112, first paragraph, as containing subject matter which is not described in the specification in such a was as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the instant application does not disclose any particular open reading frame (ORF) of any of the SEQ ID NOs:1, 4 and 8, or any particular amino acid sequence for any polypeptide that may be encoded by any one of the SEQ ID NOs:1, 4 or 8. The Examiner cited *Enzo Biochem V. Gen-Probe* with respect to his contention that the instant application does not show any correlation of structure and function for any of SEQ ID NOs:1, 4 or 8.

Claim 2 has been amended to recite only SEQ ID NOs:1 and 8. The specification discloses at p. 2, lines 23-25 that: "The Sequence Listing provides exemplary polynucleotides comprising the nucleic acid sequences of SEQ ID NOs:1-13 some of which encode the proteins comprising the amino acid sequences of SEQ ID NOs:14 and 15" (underline added). The specification further discloses at p. 23, lines 29-30 that the protein sequences of SEQ ID NOs:14 and 15 are encoded by SEQ ID NOs:1 and 8, respectively. These proteins are further characterized at p. 24, line 16 through p. 25, line 3 in terms of chemical and structural attributes and sequence homologies with known proteins. The proteins are thus adequately described such that one skilled in the art would recognize applicants possession of them and that they were derived by translation from an opening reading frame (ORF) of polynucleotide SEQ ID NOs:1 and 8, respectively. With respect to the specific ORF in each polynucleotide sequence from which the encoded proteins are derived, applicants submit that it is routine in the art to identify and translate all ORFs within a given polynucleotide sequence using analytical software such as MACDNASIS PRO software recited at p. 20, line 30 of the specification. Therefore, the specific ORF from which the polypeptides of SEQ ID NOs:14 and 15 were derived from SEQ ID NOs:1 and 8, respectively would be readily apparent to one skilled in the art based on the disclosure in the specification. The specification therefore contains a sufficient description of the polynucleotides and their encoded polypeptide sequences, as well as methods of recombinant expression of the polypeptides from their encoding polynucleotides (see specification at pp. 8-10), that one of skill in the art would recognize applicants possession of the claimed method for expressing them as recited in claim 15. Withdrawal of the rejection of claim 15 under 35 U.S.C. § 112, first paragraph is therefore requested.

35 U.S.C. § 101, Rejection of Claim 15

The Examiner has rejected claim 15 under 35 U.S.C. § 101, because the claimed invention lacks patentable utility. Specifically, the Examiner stated, the instant application does not disclose that any one of the polypeptides that may be encoded by SEQ ID NOs:1, 4 and 8 is actually expressed in vivo (the discussion in the written description rejection herein above is incorporated here). Thus, the Examiner stated, there is no disclosed utility for such polypeptides and there is no readily apparent utility for such polypeptides. In fact, the Examiner stated, there

can be no readily apparent utility for such polypeptides because the application does not provide an adequate written description of such putative polypeptides.

The amendments to claim 2 have been discussed supra. As also discussed previously under the rejection of this claim for lack of written description, the specification does adequately describe the polypeptides and their derivation from SEQ ID NOs:1 and 8. As to the expression of the polypeptides from their expressed polynucleotides in vivo, applicants submit that while steady state mRNA levels (from which the disclosed cDNAs were derived) are not always directly proportional to the amount of protein produced in a cell, mRNA levels are **routinely** used as an indicator of protein expression. Countless scientific publication have been based on data relating to mRNA levels when the polypeptide encoded by the mRNA was unknown or difficult to detect. Moreover, mRNA levels are **usually** a good indicator of protein levels in a cell. According to B. Lewin [(1997) Genes VI Oxford University Press, Inc. New York, NY] (pages attached as Exhibit A):

> Transcription of a gene in the active state is controlled at the stage of initiation, that is, by the interaction of RNA polymerase with its promoter. This is now becoming susceptible to study in the *in vitro* systems... ***For most genes, this is a major control point; probably it is the most common level of regulation.*** [page 847, emphasis added].

> But having acknowledged that control of gene expression can occur at multiple stages, and that production of RNA cannot inevitably be equated with production of protein, it is clear that ***the overwhelming majority of regulatory events occur at the initiation o transcription. Regulation of tissue-specific gene transcription lies at the heart of eukaryotic differentiation.*** [pages 847-848, emphasis added]

Thus the expression of an mRNA, such as that from which SEQ ID NOs:1 and 8 are derived, is in the vast majority of cases indicative of protein expression as well. The utility of the disclosed polypeptides are therefore derived from that of their encoding polynucleotides in the instant case, i.e., SEQ ID NOs:1 and 8. Withdrawal of the rejection of claim 15 under 35 U.S.C. § 101 is therefore requested.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections and rejections. Early notice to that effect is earnestly solicited. Applicants further request that, upon allowance of claims 1 and 2, that claims 4-12 be rejoined and examined as methods of use of the polynucleotides of claims 1 and 2 that depend from and are of the same scope as claims 1 and 2 in accordance with *In re Ochiai and Brouwer* and the MPEP § 1801.04.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Agent of Record below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

INCYTE CORPORATION

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